REMARKS

Claims 1-12, 15, 16, 18-39 and 69 remain before the Examiner for reconsideration. Claims 1, 27 and 69 are currently amended.

In the Office Action dated January 26, 2007 the Examiner indicated:

> The amendment to the claims filed 12/21/2006 has been entered. Any rejections not addressed in the office action below have been withdrawn.

However, the Examiner rejected claims 1, 10-12, 19-22, 27, 34-35 and 69 under 35 U.S.C. 102(b) "as being anticipated by Liptova et al. [sic] (Macromol. Symp. 152,139-150 (2000), cited by applicant), for the reasons set forth in the office action dated 09/21/2006." The Examiner further indicated that "a new rejection for claim 11 was necessitated by amendment." Specifically, the Examiner asserted that:

> Regarding claim 11 the examiner notes that applicants have narrowed the breath of the claim so that some species have been canceled such as carbohydrates, viral vectors, prions ect. Liptova [sic] does anticipate a carbohydrate bioactive (heparin) but heparin also anticipates an anticancer agent as evidenced by the teaching of Niers et al. (Mechanisms of heparin induced anti-cancer activity in experimental cancer models, Crit. Rev. Oncol./Hematol. (2006), doi:10.1016/j.critrevonc.2006.07.007). Neirs clearly notes that heparin demonstrated anti-cancer activity in animal tumors, thus heparin meets the limitation that the bioactive agent-is an anticancer agent. See entire document.
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> Applicants arguments/remarks filed 12/21/2006 have been fully considered but are not considered persuasive.
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> Applicant asserts that Lipatova does not disclose or suggest that heparin itself is released into the body upon degradation of the polymer but heparin would be incorporated within degradation fragments and would not be released as a result of degradation.
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> The relevance of this assertion is unclear. Firstly applicants did not disclose were to find the passage within Lipatova that the heparin would be incorporated within the degradation fragments, the examiner could not find this disclosure within the reference, thus applicants have not met their burden of showing that the heperin bond to the polymers within Lipatova would be incorporated within the degradation fragments of the polymer and not released into the body by itself. Since there is no experimental data that supports applicants viewpoint or a

> disclosure of evidence to the contrary the examiner believes that the heparin could degrade without being connected to the other degradation products through hydrolysis, therefore the limitation is considered met by the examiner. Further the claims as currently amended do not preclude that the bioactive agent would not be incorporated within degradation products, the claims as currently amended only state that the composition is biodegradable within a living organism to biocompatible degradation products including the bioactive agent, the transitional term 'including', which is synonymous with 'comprising', 'containing' or 'characterized by', is inclusive or open ended and does not exclude additional elements in the prior art. Thus the claim language does not preclude that the bioactive could be connected to degradation products. Furthermore the limitation that the polymer is biodegradable within the body and the released bioactive agent affecting at least one of biological activity or chemical activity in the host organism is an intended use of the polyurethane, ('where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation'); Kropa v. Roble, 187 F.2d at 152, 88 USPQ2d at 480-81. Therefore since the polyurethane is synthesized in the same way is useful as an implant and is the same composition as applicants currently claimed polyurethane composition the limitations in the claims are met. Lastly since the claimed polyurethane composition is the same as applicants currently claimed invention any composition with the same composition as applicants claimed invention would inherently have the same degradation properties when inserted into the body.

Applicants respectfully traverse the Examiner's rejection.

Initially, Applicants note that claims 1, 27 and 69 have been amended to even more clearly indicate that the polyurethane compositions of the present invention are biodegradable within a living organism to release the bioactive agent. Applicants respectfully assert that the release of the bioactive agent itself was clear from the claims and specification as filed. Indeed, the claims indicated that the released bioactive agent could affect at least one of biological activity or chemical activity in the host organism. Contrary to the Examiner's assertion, the recitation of "the released bioactive agent" does not appear in the preamble of the claims and is not merely a statement of purpose or intended use.

Without any support in Lipatova, the Examiner asserts that "the examiner believes that the heparin could degrade without being connected to the other degradation products through hydrolysis" Indeed, there is no specific disclosure in Lipatova of the manner in which heparin is incorporated into the polymers of Lipatova. It is not apparent, for example, that heparin itself is reacted with a multifunction isocyanate as required of the biologically active agents of the present

invention. Moreover, the lack of instruction as to how the heparin is incorporated within the polyurethanes of Lipatova makes it impossible to determine if heparain would be an eventual degradation product thereof and how long it would take for such a degradation to occur. In that regard, heparin is incorporated in the polymer or Lipatova to improve hemocompatibility of the polymer itself and not for any biological after degradation. Once again, there is no disclosure or suggestion in Lipatova that heparin itself is released into the body upon degradation of the polyurethane polymer matrix of Lipatova or that such a result is even desirable. Indeed, it may be undesirable to have the anticoagulant heparin released into the body in the creation of artificial blood vessels, which is the stated aim of the work of Lipatova.

Moreover, Applicants have further amended claims 1, 27 and 69 the multifunction isocyanate compound is formed via conversion of amine groups of a biocompatible compound having at least two amine groups to isocyanate groups. The use of such multifunctional isocyanate compounds, distinguishes the composition of the present invention from those of Lipatova. Unlike the composition of Lipatova, the polyurethanes of the present invention degrade to release the bioactive agent within a timeframe such that the bioactive agent is released within the body to affect at least one of biological activity or chemical activity in the host organism.

Applicants respectfully assert that the Examiner has failed to meet the burden of establishing anticipation over Lipatova.

The Examiner also rejected Claims 1-4, 7-8, 12, 19, 22, 27-30, 33 and 69 under 35 U.S.C. 102(e) "as being anticipated by Woodhouse et al. (US 6,221,997 B1, cited by applicant), for the reasons set forth in the office action dated 09/21/2006." Specifically, the Examiner asserted that:

> Applicants appear to state that as currently amended Woodhouse does not anticipate the claimed invention because amino acids are not included in the Markush group of independent newly amended claims 1, 27 and 69.
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> The relevance of this assertion is unclear, clearly Woodhouse discloses that the amino acid group may be joined together to form an oligopeptide, which would meet the limitation that the bioactive agent is a peptide or a polyamino acid.

Applicants respectfully traverse the Examiner's rejection.

Woodhouse discloses a biodegradable polyurethane material having a backbone containing at least one amino acid group that is in a condition rendering it "recognizable" by a biological agent. The term "'biological agent' is intended to refer to such things as molecules that bind or recognize other polypeptides or amino acids." Col. 4, lines 29-31. Enzyme recognition is disclosed to be the preferred embodiment. The "term amino acid group" as used in Woodhouse "includes at least one or more amino acid residues, that is as many as would be suitable for enzyme recognition, such as less than 20, preferably in some cases less than 10, preferably in some cases less than 5." Col. 4, lines. In the disclosed embodiments, hydrolyzable ester linkages are introduced into the polyurethanes adjacent the recognizable amino acids. For example, carboxyl terminals of two amino acids and the hydroxy functions of two non-toxic diols (such as 1, 4 cyclohexane imethanol) are reacted via an esterification reaction. See col. 8, lines 53-58. Unlike the present invention, nowhere, does Woodhouse disclose or suggest reacting isocyanate groups of at least one multifunctional isocyanate compound with at least one bioactive agent to form a polyurethane that is biodegradable within the body to release the bioactive agent. The amino acid groups of Woodhouse, whether comprising a single amino acid, or joined together to form an oligopeptide or polyamino acid as suggested by the Examiner, are not reacted with a multifunctional isocyanate as set forth in the present claims.

Moreover, in embodiments in which a plurality of amino acids are joined together in Woodhouse to from an oligopeptide or polyamino acid as suggested by the Examiner, such oligopeptide or polyamino acid may be altered/destroyed during the enzymatic recognition described in Woodhouse (for example, via protease recognition). See, for example, col. 5, lines 23-37. In such a case, the oligopeptide or polyamino acid would not be released into the body upon degradation of the polymer. Moreover, Woodhouse describes specifically only the reaction/esterification of L-phenylalanine and L-lysine (amino acid groups under the definition of Woodhouse) and 1,4 cyclohexane dimethanol to form a chain extender for use in formation of the polyurethanes of Woodhouse. Applicants respectfully assert that it is not clear how an oligopeptide or a polyamino acid would function in the polyurethanes of Woodhouse or that Woodhouse is enabling for the use of such oligopeptides or polyaminoacids in the polyurethanes thereof.

Claims 1-12,15-16,18-39 and 69 are also rejected by the Examiner under 35 U.S.C. 103(a) "as being unpatentable over Zhang et al. (Biomaterials 21 (2000) 1247-1258, cited by applicants), for the reasons set forth in the office action dated 09/21/2006." Specifically, the Examiner asserted that:

> Applicants assert that Liptova [sic] does not cure the deficiencies of Zhang in which applicants assert does not disclose covalent attachment of a protein or any other bioactive group to the polyurethane. Furthermore applicants assert that Lipatova does not disclose or suggest that heparin itself is released into the body upon degradation of the polymer and that heparin is not a protein but a glycosaminoglycan.
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> Firstly the examiner acknowledges the misprint/mistake in the previous office action that heparin is a protein, indeed heparin is a glycosaminoglycan but heparin is still obviously a bioactive agent because it is a glycosaminoglycan, glycosaminoglycans are polysaccharides and polysaccharides are carbohydrates, which as claimed by applicants are bioactive agents. From the above arguments Liptova [sic] does disclose a heparin containing polyurethane in which the bioactive would be released into the body upon degradation of the polymer. Lastly even if Zhang is not enabling for covalent attachment of proteins on the polyurethane it still would have been obvious to the skilled artisan to combine the disclosures of Zhang and Litova [sic] to synthesize a biodegradable polyurethane containing a bioactive agent (heparin) that may be applied as a prosthetic appliance in direct contact with living tissues. The two references are obviously combinable with each other because they are directed to the same general field of endeavor, polyurethane compositions for the treatment of living tissues.

Applicants respectfully traverse the Examiner's rejection.

Initially, Applicants note that the Examiner's rejection of claims 1-12, 15-16, 18-39 and 69 is over Zhang et al. However, the Examiner seems to admit that Zhang et al. is not enabling for covalent attachment of proteins within the polyurethane thereof. It seems from the Examiner's assertions that the rejection under section 103 should have been made over Zhang et al. in view of Lipatova. Applicants address the rejection below as if made over Zhang et al. in view of Lipatova.

As admitted by the Examiner in the Office Action dated September 12, 2006, "Zhang while disclosing the peptide based urethane polymer may allow incorporation of proteins of interest such as cell attachment and/or growth factors does not give any working examples." Once again, Zhang does not disclose even what is meant by incorporation of proteins. In that regard, in the present invention an isocyanate group of at least one multifunctional isocyanate compound is reacted with

the bioactive agent, thereby covalently bonding the bioactive agent within the polyurethane composition. There is no disclosure or suggestion of the covalent attachment of a protein or any other bioactive group within the polymer of Zhang or how a protein could be covalently incorporated within the polymer matrix of Zhang. The disclosure of Zhang is not enabling for the covalent incorporation of a protein therein. Moreover, a protein can be physically "incorporated" within the polymer matrix of Zhang without covalent attachment of the protein within the polymer via, for example, an encapsulation or entrapment process. Furthermore, there is no disclosure of how or if the polymer of Zhang would degrade to release a protein (or other bioactive agent) as a degradation product should such a protein (or other bioactive agent) be covalently incorporated into the polymer thereof.

For the reasons set forth above, Lipatova does not overcome the deficiencies of Zhang. Once again, the manner in which heparin is covalently incorporated into the polymers of Lipatova is not apparent. Once again, it is not apparent that heparin itself is reacted with a multifunction isocyanate as required of the biologically active agents of the present invention. Further, the lack of instruction as to how the heparin is incorporated within the polyurethanes of Lipatova makes it impossible to determine if heparain would be an eventual degradation product thereof and how long it would take for such a degradation to occur. Applicants respectfully assert that it would not have been obvious to a skilled artisan to combine the disclosures of Zhang and Lipatova to arrive at the present invention in which a bioactive agent is reacted with isocyanate groups of at least one multifunctional isocyanate compound to form a polyurethane that degrades to release the bioactive agent within the body.

In view of the above amendments and remarks, Applicants respectfully requests that the Examiner, indicate the allowability of the Claims, and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,
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